HIGH SPEED PARALLEL MOLECULAR NUCLEIC ACID SEQUENCING

Abstract

A method and device is disclosed for high speed, automated sequencing of nucleic acid molecules. A nucleic acid molecule to be sequenced is exposed to a polymerase in the presence of nucleotides which are to be incorporated into a complementary nucleic acid strand. The polymerase carries a donor fluorophore, and each type of nucleotide (e.g. A, T/U, C and G) carries a distinguishable acceptor fluorophore characteristic of the particular type of nucleotide. As the polymerase incorporates individual nucleic acid molecules into a complementary strand, a laser continuously irradiates the donor fluorophore, at a wavelength that causes it to emit an emission signal (but the laser wavelength does not stimulate the acceptor fluorophore). In particular embodiments, no laser is needed if the donor fluorophore is a luminescent molecule or is stimulated by one. The emission signal from the polymerase is capable of stimulating any of the donor fluorophores (but not acceptor fluorophores), so that as a nucleotide is added by the polymerase, the acceptor fluorophore emits a signal associated with the type of nucleotide added to the complementary strand. The series of emission signals from the acceptor fluorophores is detected, and correlated with a sequence of nucleotides that correspond to the sequence of emission signals.